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Coronary Artery Calcification Is Often Unreported in CT Pulmonary Angiograms in Patients With Suspected Pulmonary Embolism: An Opportunity to Improve Diagnosis of Acute Coronary Syndrome

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Abstract

Objective: In patients with suspected pulmonary thromboembolism (PTE), coronary artery calcification (CAC) can be an incidental finding in CT pulmonary angiograms. We evaluated the frequency of unreported CAC and its association with diagnosis of acute coronary syndrome (ACS).

Methods: The data of 469 consecutive patients who were referred to the emergency radiology department for CT pulmonary angiography because of suspicion for PTE were reviewed. Radiology reports were rechecked, and positive CAC findings were recorded. All CT pulmonary angiograms were re-evaluated by one radiologist, and CAC findings were recorded. The rate of ACS and PTE as final diagnosis for that hospital admission was calculated. The association between CAC and ACS diagnosis was assessed in different subgroups of patients.

Results: About 11.1% of patients had PTE and 43.8% had CAC. CAC was significantly higher in patients with ACS diagnosis than those without (56.2% vs. 40.4%; OR = 1.9). There was a strong positive association (OR = 3.5) between CAC and ACS in younger patients (age ≤ 45 in men, age ≤ 55 in women); those without PTE (OR = 2.15); and those without cardiometabolic risk-factors (OR = 3.8). CAC was unreported in 45% of patients with positive CAC (n = 98). ACS was the final diagnosis in 31.6% of patients with unreported CAC. There was a significant association between CAC and ACS in patients with unreported CAC (OR = 2.18). This association was more prominent in the above subgroups.

Conclusions: CAC is often unreported in CT pulmonary angiograms. CAC is a significant predictor of ACS, particularly in younger patients and those without PTE and cardiometabolic risk-factors. Especially in these sub-groups, radiologists should assess CAC findings.

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Glossary of Abbreviations

ACS: Acute coronary syndrome

AHA: American Heart Association

CABG: Coronary artery bypass grafting

CAC: Coronary artery calcification

CACS: Coronary artery calcification score

CAD: Coronary artery disease

CI: Confidence interval

CT: Computed tomography

ECG: Electrocardiogram

HIPAA: Health Insurance Portability and Accountability Act

IRB: Institutional Review Board

NSTEMI: Non-ST-elevation myocardial infarction

OR: Odds ratio

PCI: Percutaneous coronary intervention

PTE: Pulmonary thromboembolism

QPID: Queriable patient inference dossier

SD: Standard deviation

STEMI: ST-elevation myocardial infarction

Section 1: Introduction

Coronary artery disease (CAD) is an important contributor to cardiovascular disease burden, accounting for one out of every five deaths in the United States in 2005 [1]. In 2009, estimates show 785000 Americans will have a new coronary attack, and 470000 will suffer a recurrent one [1]. Reducing the disease burden of CAD and managing progression of the disease is an important goal in order to decrease deaths due to cardiovascular disease and lower the overall financial and clinical impact of CAD [2].

Radiologic imaging is often an important component of diagnosis for many clinical questions. Imaging may unearth incidental findings, which are sometimes defined as “an incidentally discovered mass or lesion, detected by an imaging examination performed for an unrelated reason” [3]. It is not always clear, however, whether something is unrelated. Moreover, there is very little research or guidance in how or whether to pursue incidental findings [3]. Because of this, recommendations are often inconsistent [3]. Additionally, as imaging utilization has increased, the number of incidental findings has also risen [3]. Incidental findings can be beneficial through an improvement in timely diagnosis and treatment for patients; however, incidental findings may also be harmful to patients by encouraging unnecessary tests and/or treatments [4]. Therefore, gaining a better understanding of when and how specific radiologic findings may be useful and clinically relevant is an important goal.

Incidental cardiac findings in particular on chest and abdominal scans offer a potential avenue for having a broad impact on CAD. Chest computed tomography (CT) examinations for non-cardiovascular purposes can contain valuable information about atherosclerosis [5]. Coronary artery calcification (CAC) is one cardiac finding that can be visualized on chest CT noninvasively [6]. CAC includes atherosclerotic and medial artery calcification [6].

Atherosclerotic calcification is within the media and is the result of inflammatory mediators and lipid content causing vascular smooth muscle cells to undergo osteogenic differentiation, whereas medial CAC is associated with age, diabetes, and chronic kidney disease [6]. Plaque burden is associated with the extent of CAC [6]. CAC can also be scored, and the coronary artery calcification score (CACS) can be informative in assessing risk for coronary heart disease events [6-8]. Incidentally detected CAC on diagnostic chest CT is a significant predictor of cardiovascular disease events [9], and it can impact clinical care and management [10, 11]. CAC is associated with higher rates of arrhythmias, ischemia, hypotension, myocardial infarction, and death [12, 13]. Acute ischemic heart diseases have been associated with a significantly higher CAC score than that in normal patients, although acute ischemic heart diseases have also been associated with a significantly lower CAC score than that of chronic ischemic heart diseases [14]. A recent paper by Puchner et. al showed that high-risk plaques on coronary CT angiography were a significant predictor of ACS independently of clinical risk assessment and significant CAD [15].

A common clinical scenario where CT examinations are used in clinical diagnosis is when a patient is suspected of having a pulmonary thromboembolism (PTE). Patients with PTE present with a wide spectrum of clinical symptoms and findings [16]. Common symptoms include pleuritic pain, chest pain, dyspnea, orthopnea, and cough, amongst others [16]. Common signs are tachypnea and tachycardia [16]. All patients with dyspnea and/or chest pain should be suspected of having potential pulmonary embolism [17]. The array of clinical symptoms, acute presentation, and often nonspecific findings allow for PTE to be a great imitator of other conditions. Symptoms of PTE, especially chest pain and dyspnea, can be challenging to differentiate between ACS [18]. ACS is a major cause of morbidity and mortality for patients [19]. Management for ACS should be initiated as promptly as possible [18]. Because of the

similar presentation between PTE and ACS along with the morbidity and mortality associated with ACS, ACS is an important component of the differential diagnosis in patients with possible PTE. Quick differentiation between PTE and ACS is clinically very important because appropriate therapeutic management differs between the two conditions, and both can be life threatening [18].

Given the significance of prompt diagnosis in both ACS and PTE, improving the diagnosis of both is clinically important. PTE diagnosis can be notoriously challenging. Algorithms exist to aid in diagnosis of PTE, but when to initiate these algorithms does not have a clear recommendation [20]. Moreover, some criteria for aiding in assessing the clinical probability that a patient has a PTE are subjective. For example, the modified Wells' criteria contains "likelihood of an alternative diagnosis" as one of its criteria [20]. When suspected probability of PTE is high enough, CT pulmonary angiography is the recommended test of choice to diagnose PTE [17]. Because of this along with the difficulty of assessing probability that a patient has a PTE, patients with high enough clinical suspicion of pulmonary thromboembolism are routinely referred for CT pulmonary angiography as a part of their initial clinical evaluation [21].

In contrast, the diagnosis of ACS can be more straightforward and accurate. ACS spans a spectrum of diseases that include unstable angina, non-ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI) [22]. Unstable angina by definition is EKG changes suggestive of ischemia without evidence of myocardial necrosis via biomarkers [23]. STEMI is diagnosed by EKG, whereas NSTEMI is diagnosed by a combination of biomarkers and EKG changes [23]. Cardiac troponin is highly sensitive and specific. Analyses of troponin biomarkers have demonstrated a sensitivity of 100.0%, a specificity of 34.0%, and a negative predictive value of 100.0% with a cardiac troponin T cutoff of 3 ng/L and a sensitivity of 85.4%, specificity of 82.4%, and negative predictive value of 96.1% with a cutoff of 14 ng/L [24].

Despite the availability of troponin biomarkers, the diagnosis of ACS in the emergency department setting remains difficult. [25]. ACS diagnosis is missed in 2-4% of patients [25]. In particular, the presentation of patients with chest pain, a non-diagnostic EKG, and normal troponins represents a challenge for providers, and some of these patients at long-term follow up develop cardiac events [25]. Importantly, the EKG does not adequately depict the posterior and lateral walls and may not rule out ischemia in those regions [23]. Additionally, it may take as many as six hours following onset of myocardial damage for the troponin to rise [23]. Moreover, because troponin levels can remain increased for two weeks following damage to the myocardium, diagnosis of reinfarction can be difficult [23].

Because of the overlap in clinical presentation between ACS and PTE and the diagnostic uncertainty that may occur in both conditions, the patient population undergoing CT pulmonary angiography is one where prediction of ACS risk based on CT pulmonary angiograms is potentially of great clinical value. CT pulmonary angiograms demonstrate a high yield of incidental cardiac findings [26]. However, radiologists do not consistently report these incidental findings, and it is not always clear which findings should be reported. The purpose of this study was to evaluate the frequency of unreported CAC and its association with ACS in patients with suspected PTE. We tried to address several questions. By failing to report CAC, are radiologists missing a potential diagnosis of ACS? What is the frequency of ACS diagnosis in patients with unreported CAC? In patients with what characteristics should a radiologist consider CAC as a stronger correlate of ACS? Ultimately, should the presence of CAC be included in the radiology report? To determine the answer to these questions, we evaluated the association between CAC and ACS diagnosis in different subgroups of patients.

Portions of this work have been previously published (Johnson et. al 2014) [27].

Section 2: Methods

We performed a retrospective analysis of 469 consecutive patients who were referred to the emergency radiology division for pulmonary CT angiography of suspected PTE over a period of 3 months from January to March 2010. This study followed the HIPAA guidelines and was approved by our institutional review board.

Data of all patients who underwent pulmonary CT angiography for evaluation of PTE were included. Patients underwent a standard-protocol pulmonary CT angiography examination on a 64-MDCT unit (64-slice LightSpeed VCT, GE Healthcare) or a 16-MDCT unit (LightSpeed Pro 16 VCT, GE Healthcare). Patient data were obtained using a health intelligence platform (Queriable Patient Inference Dossier, QPID) that includes an electronic health record search engine in our hospital. For patients who had undergone more than one CT examination during the study period, the first one was selected for analysis. The radiology reports of the pulmonary CT angiography examinations were reviewed to see whether CAC was reported in either the Findings or Impression sections. A radiologist with 10 years' experience in emergency radiology reevaluated all the CT examinations and recorded positive CAC findings. CAC was positively identified when observed in the anatomic sites of the coronary arteries.

PTE or ACS was identified as the clinical diagnosis if either was indicated in the medical report of the patient as the final diagnosis for that hospital admission. A PTE diagnosis was based on suggestive medical history, physical examination, and positive findings on pulmonary CT angiography. An ACS diagnosis was based on suggestive physical examination, medical history, positive ECG findings, and changes in cardiac enzyme levels. The following data were obtained from patients' medical histories: personal history of CAD, myocardial infarction, stent placement for reasons related to CAD, coronary artery bypass graft, diabetes, hypertension,

smoking, and hypercholesterolemia or hyperlipidemia; family history of CAD; and obesity.

Patients without cardiometabolic risk factors were defined as those who were not obese and did not have a history of diabetes mellitus, hypertension, hyperlipidemia, or smoking.

Statistical Analysis

The statistical analysis was performed using SPSS software (version 19.0, SPSS). Continuous variables are expressed as means \pm SD. Continuous variables were compared between groups using an independent-sample Student *t* test, and categoric variables were compared using a chi-square analysis or the Fisher exact test as appropriate. The association between CAC and ACS was evaluated using univariate and multivariate logistic regression models. The odds ratio (OR) for the prediction of ACS was calculated and reported along with 95% CIs. The association between CAC and ACS was evaluated in different age categories (age \geq 70 years in both sexes, because ACS is associated with aging-related calcification; age $>$ 45 in men and $>$ 55 years in women, because ACS is associated with increased cardiometabolic risk [28]. The level of significance was set at $p < 0.05$.

A report of these methods has been previously published (Johnson et. al 2014) [27].

Section 3: Results

Table 1 demonstrates the demographic and clinical characteristics of the studied patients. On CT examination, 52 patients had positive findings for PTE (11.1%) and 206 (43.8%) had positive CAC findings. Of the patients with positive findings for CAC, 14.6% had PTE and 28.6% had positive findings for ACS, which was significantly higher than in patients without CAC (8.4% PTE and 17.5% ACS). Patients with CAC had a significantly higher frequency of diabetes, hyperlipidemia, hypertension, smoking, and personal history of CAD (Table 1).

Coronary Artery Calcification in Radiology Reports of Patients

CAC was reported in the radiology findings of 114 patients (24.3% of all patients). Among these cases, CAC was reported in the impression section of the radiology report in 9 patients (1.9% of all patients; 4.4% of patients with positive report of CAC). In only 55.3% of patients with CAC was this finding reported in the radiology assessment of the patient (114 out of 206 patients); in other words, CAC was not reported for 44.7% of patients with positive findings for CAC ($n = 98$). ACS was the final diagnosis in 31.6% (31/98) of patients with unreported CAC. There were no false positive reports of CAC in the impression or findings sections of the radiology reports.

In patients for whom CAC was not reported in the radiology findings, CAC was significantly associated with ACS (ACS in patients with CAC: $n = 31$, 31.6%; ACS in patients without CAC: $n = 45$, 17.5%; OR = 2.2; 95% CI = 1.3-3.7; $p = 0.004$). This association was more prominent in patients without cardiometabolic risk factors ($n = 6$, 33.3% vs. $n = 15$, 9%; OR = 5.0; 95% CI = 1.6-15.3; $p = 0.002$); patients without PTE ($n = 30$, 34.5% vs. $n = 41$, 17.4%; OR = 2.5; 95% CI = 1.4-4.4; $p = 0.001$); and patients who were less than 70 years old ($n = 21$, 30.8% vs. $n = 38$, 15.4%, OR = 2.5; 95% CI = 1.3-4.6; $p = 0.004$) (Figure 2).

Association of CAC with ACS

Table 2 presents the association of CAC detected on pulmonary CT angiograms with ACS in different subgroups of patients, including patients with and those without a personal history of CAD, cardiometabolic risk factors, and PTE and patients younger than 70 years old and those 70 years or older. There was a significant positive association between CAC and ACS in patients without a personal history of CAD (OR = 1.9), those without cardiometabolic risk factors (OR = 3.8), those less than 70 years old (OR = 2.35), and those without PTE (OR = 2.15). In patients 70 years old or older, CAC was significantly associated with a lower chance of ACS (OR = 0.25). There was no association between ACS and CAC in patients with a personal history of CAD, patients with cardiometabolic risk factors, or those with PTE.

In all the patients together, CAC was significantly associated with ACS (OR = 1.9; 95%CI = 1.2-2.9; P = 0.004) (Table 2). In a multivariate logistic regression analysis with sex, age category, personal history of CAD, and PTE as covariates, CAC was significantly associated with ACS (OR = 1.8, 95%CI = 1.1-3.0; P = 0.025).

We further explored the effect of age on the association between ACS and CAC by evaluating this association in three age categories. As presented in Figure 3, in the youngest age category (age \leq 45 years in men and age \leq 55 years in women), there was a strong direct association between ACS and CAC (OR = 3.5). In the middle category for age, this association was weak (OR = 1.4), and in the oldest category for age (age \geq 70 years), the association was significantly inversed (OR = 0.25) (Figure 3).

A report of these results has been previously published (Johnson et. al 2014) [27].

Section 4: Discussion, Future Work, My Role, and Conclusions

Discussion and Future Work

Incidental findings on imaging are an important concern in health care for clinical and financial reasons. When incidental findings should be reported and how they should be followed up is not always clear [3]. CAC is one such incidental finding in radiologic studies that may be of interest clinically. Our results are important because they demonstrate possible clinical impact of incidentally detected CAC in patients undergoing CTPE for suspected PTE. Because CT pulmonary angiograms are the recommended test for PTE diagnosis, suspected PTE patients are usually referred for these radiologic examinations in emergency rooms as a part of their initial medical evaluations, when many work-ups are incomplete. As a result of the overlap of clinical presentation and the challenge of diagnosing PTE and ACS, any potential contributor to assessing the possibility of ACS in patients evaluated for PTE is clinically relevant. Our results showed that in young patients (especially age ≤ 45 in men and age ≤ 55 in women), those without past history of CAD, and those without cardiometabolic risk factors, coronary artery calcification is an independent predictor of ACS. These results suggest that in certain groups of patients where ACS is a less likely diagnosis clinically because of age, the absence of a personal history CAD, or the absence of cardiometabolic risk factors, the presence of CAC on CTPE can potentially be clinically useful.

We evaluated the association between CAC and ACS in different strata of patients. This analysis revealed that there is an independent association between CAC and ACS in patients without PTE and cardiometabolic risk factors. An interesting finding was the effect modifier role of age. CAC was positively associated with ACS in younger patients, whereas,

in patients with age greater than or equal to 70 years, there was an inverse association between CAC and ACS. Additionally, our study showed that in patients without history of cardio-metabolic risk factors, incidental CAC has a stronger association with ACS diagnosis.

Young patients, patients without history of CAD, and patients without cardiometabolic risk factors are less likely to be suspected of having ACS given the absence of expected risk factors. Because of the subjective nature of PTE diagnosis and the overlap of presentation with that of ACS, these patients may undergo CT pulmonary angiogram to evaluate for PTE. Because CAC is associated with ACS in these patient populations, the presence of CAC on CT pulmonary angiogram should be a clinical indicator to evaluate these patients closely for ACS. These patients groups may be vulnerable to having undiagnosed ACS given that they do not have tradition risk factors, and the presence of CAC could aid in avoiding missed ACS diagnoses. Additionally, the presence of CAC in these patient groups may change the way providers view the ACS risk in these patients over the long term, though further studies are needed to evaluate CAC's impact on diagnosis and impact on management of long term ACS risk. The major potential clinical utility of detecting CAC on CT pulmonary angiography in young patients, patients without history of CAD, and patients without cardiometabolic risk factors is that the presence of CAC may transform the perception of providers. Instead of considering these patient populations to be at low risk for ACS, providers may view them as more likely to have ACS and be more vigilant in assessing for ACS.

Our results may offer some insight regarding the formation of CAC in different patient populations. Atherosclerotic calcification and medial CAC have different mechanisms of formation [6]. The former occurs via osteogenic differentiation of vascular smooth muscle cells within the media, whereas the latter is associated with aging and comorbidities [6]. The association of ACS with CAC in patients that are young and without cardiometabolic risk factors

suggests that the detected CAC in these patient populations occurs via a mechanism of atherosclerotic calcification, or at least to a greater degree than in patients who are older and with cardiometabolic risk factors. Because the association between ACS and CAC was not as strong in patients with cardiometabolic risk factors, it is likely that the detected CAC in this population is medial CAC related to comorbidities. For patients with an age greater than or equal to the age of 70, the inverse association of CAC and ACS suggests that age along with comorbidities is responsible for the presence of CAC. Presumably, patients with a history of CAD will have CAC related to atherosclerotic calcification, so it may be that patients without a history of CAD are more likely to have CAC that is associated with ACS and relevant to their current clinical presentation as opposed to patients with a prior history of CAD, where the presence of CAC is chronic, may be more complicated to interpret, and is less likely to be associated with a current presentation of ACS. Overall, these differing mechanisms may offer insight into why CAC is most useful in patients who are young, without a history of CAD, and without cardiometabolic risk factors. In these patients, the presence of CAC is more likely to reflect a mechanism of atherosclerotic calcification and is more likely to be associated with a presentation of ACS; in contrast, the presence of CAC in older patients and those with cardiometabolic risk factors likely reflects a mechanism of medial CAC from aging and/or comorbidities and is not associated with ACS.

Our results demonstrating the association of CAC and ACS are relevant to the specific clinical scenario of patients undergoing CTPE for suspected PTE. Whether or not these results are generalizable beyond this clinical scenario to other patient populations is unclear and should be evaluated with additional studies in the future. The patient population studied had a high prevalence of ACS, as the patients in our study without CAC had a 17.5% rate of ACS. As a comparison, Towfighi and colleagues examined NHANES cross sectional national surveys and found that 2.2% of men and 1.0% of women age 35 to 54 reported a history of MI in NHANES

1999-2004 [29]. The patient population undergoing CTPE for suspected PTE in this study is a substantially different population with higher than average rates of ACS, and it is possible that incidental CAC has a higher utility in these patients than in other patient populations.

Nonetheless, our results may suggest that the presence or absence of CAC could potentially have clinical utility in other clinical scenarios as an incidental finding.

Another important consideration is that ACS in general is an accurate diagnosis [24]. Troponin biomarkers are effective tools for diagnosis of MI. However, although diagnosis in ACS is accurate, it is not perfect, as EKG and biomarkers both have weaknesses in diagnosis.

Unstable angina by definition relies on EKG for diagnosis. EKG has a low sensitivity [25], it may not rule out ischemia in certain myocardial regions [23], and acute pulmonary embolism can also cause EKG abnormalities to emerge [18]. Biomarkers can be elevated in situations where there is not an acute myocardial infarction [30], and diagnosing reinfarction can be challenging given troponins can remain elevated for up to two weeks [23]. Thus, patients presenting with symptoms but no objective evidence of ACS are still a diagnostic dilemma [15]. Imaging findings such as CAC on CTPE may play a role in aiding providers in assessing the likelihood of ACS versus other diagnoses in situations where EKG and biomarkers do not reveal a clear diagnosis or are complicated by other factors. In all patients with possible ACS, timely diagnosis and early initiation of therapy is important given the morbidity and mortality associated with the disease, Improving the promptness of diagnosis is a significant goal that may be aided by the presence of CAC on CTPE.

The variety of clinical presentations as well as the morbidity and mortality associated with ACS create a difficult clinical scenario when the diagnosis of ACS is in question. Troponin assays may not become elevated until six hours following the onset of myocardial necrosis [23]. In the setting of a nondiagnostic EKG, this creates a potential window of several hours where ACS

may be occurring or evolving but is not reflected in a positive result in the troponin assay. This situation may be referred to a possible evolving ACS. In this time, a patient may undergo testing for alternative diagnoses, including a CT pulmonary angiogram for evaluation of possible PTE. This is a clinical situation where CAC could impact clinical care. The presence of CAC on imaging in the appropriate patient populations (such as young patients, those without a history of CAD, and those without cardiometabolic risk factors) may guide care providers in assessing the likelihood of ACS as the clinical diagnosis. Care providers may initiate earlier therapies or adjust diagnostic and/or therapeutic decisions based on the likelihood of ACS as the diagnosis. In contrast, the absence of CAC may offer additional reassurance to providers that ACS is less likely and further encourage investigation into alternative causes of the patient's presentation. Further studies are needed to determine exactly how diagnostic and therapeutic decisions should be adjusted in the setting of positive CAC in the appropriate patient populations.

Understanding the true impact CAC may have on clinical care will require further investigation. However, our results suggest some possibilities for how the presence of CAC could impact clinical care in the short term and in the long term. As discussed previously, the presence of CAC in patients who are younger, who do not have a personal history of CAD, and who do not have cardiometabolic risk factors is associated with ACS. In these patients, if CAC is present on CT pulmonary angiography care providers may adjust clinical care decision-making given the higher likelihood of ACS as the clinical diagnosis. In particular, short term clinical decision making may be most impacted by the presence or absence of CAC on CT pulmonary angiography in situations where ACS is a diagnostic possibility but the diagnosis remains unclear based on EKG and troponin assay.

One specific clinical scenario involves the presentation of patients with chest pain in the emergency department, where PTE and ACS are both diagnostic possibilities. The diagnostic

dilemma of patients in the emergency department with chest pain and unrevealing information from EKG and biomarkers may be benefited from CT pulmonary angiography, where information about PTE and CAC can affect the likelihood of both diagnoses simultaneously. Possibly even cases of missed ACS diagnosis could be prevented through detection of CAC. In addition to short term clinical management, the presence of CAC on CT pulmonary angiography may also impact long term clinical care. Younger patients, those without history of CAD, and those without cardiometabolic risk factors who are found to have CAC on CT pulmonary angiography have a higher odds ratio for having ACS. Though further studies are necessary to understand future risk of ACS in this patient population, it is possible that these patients are at higher risk for future ACS, and care management may be impacted by the knowledge that CAC is present.

Little data and/or guidance is given regarding the reporting practices of incidental findings [3]. The purpose of the radiology report is to provide clear communication about imaging results to providers, but there is a large amount of variation in reporting practices among radiologists [31]. The body of the radiology report should contain imaging findings [31]. It is difficult to find clear guidance on what should and should not be included in the findings. ACR guidelines state that in the findings the “report should use appropriate anatomic, pathologic, and radiologic terminology to describe the findings” [32]. In contrast, the impression section of the radiology report is what is primarily viewed by the ordering physician [31]. The impression section should contain critical findings and contain a specific diagnosis if possible [31]. ACR guidelines recommend that in the impression “a specific diagnosis should be given when possible, [a] differential diagnosis should be rendered when appropriate, [and] follow-up or additional diagnostic studies to clarify or confirm the impression should be suggested when appropriate” [32]. The findings of the radiology report should characterize the radiologic anatomy, and the impression of the radiology report should offer clear communication of all potentially relevant

findings as well as offer a differential diagnosis and ultimate diagnosis if possible.

Despite the limitations of this study, the significant association between CAC and ACS offers reason to encourage increased vigilance in looking for CAD in patients undergoing CT pulmonary angiography. Given our results, we suggest that the presence or absence of CAC should be reported in pulmonary angiograms in both the findings and impression of radiology reports. We suggest that the presence or absence of CAC should be reported in the findings section, as it is a component of the anatomy visualized during the CT pulmonary angiography examination.

The ultimate goal of the radiology impression is to communicate important clinical findings and guide diagnosis. More importantly, we suggest that when CAC is present or absent, it should be included in the impression because it is a pathological anatomic finding and its presence or absence may have an impact on clinical care, diagnosis, and the likelihood of ACS.

In light of the possible utility of CAC for short and long term clinical care, an assessment of CAC reporting rates is important. Our results showed that CAC is unreported in about half of patients with positive CAC findings. In unreported cases, CAC was significantly associated with ACS as final diagnosis. This indicates radiologists are missing a potential diagnosis for these patients, and potentially an avenue for impacting clinical care is being missed. Why CAC was unreported at such a high rate in the findings is unclear.

Reporting incidental CAC could possibly have an impact on short- and long-term clinical care of patients undergoing CTPE for possible PTE. Less than 5 percent of patients with CAC had this reported in the impression section of the radiology reports. Since the impression section of the radiology report is read more frequently and thoroughly than the findings section and is

ultimately the part of the radiology report with the goal of providing effective communication to ordering physicians, increasing the rates of CAC reported in the impression may be an important goal for impacting clinical care as much as possible. This is especially true for younger patients, those without a history of CAD, and those without cardiometabolic risk factors, where reporting the presence of CAC may have the greatest clinical impact. Similarly, why the impression reporting rate for CAC in CT pulmonary angiograms is so low is unclear. One possibility is that incidentally detected CAC on CT pulmonary angiograms is thought to be irrelevant to diagnosis or insignificant as a clinical finding.

An important limitation relevant to the interpretation of our results is the use of retrospective data; therefore the direction of the observed associations cannot be inferred, and no conclusions can be drawn about causality. Future research could include a follow-up study to evaluate the association of CAC incidental finding with short-term and long-term cardiac outcomes, especially assessing long-term ACS risk in different patient populations with detected CAC. In particular, our study did not evaluate the possibility of incidentally detected coronary artery calcification leading to a new diagnosis of coronary artery disease and how that diagnosis could impact long-term medical management and prevention of future adverse outcomes such as ACS. Additionally, our study did not evaluate whether incidentally detected CAC prevents any missed diagnoses of ACS. Therefore, another interesting future study could involve assessing radiographic findings and the role of new diagnosis of coronary artery disease. How primary care providers alter long term risk management in patients with newly detected coronary artery disease is another important question that could be evaluated in a follow up study.

Our results provide new insights on the role of radiology in assessment of suspected PTE patients. CT technology is improving at a rapid pace. With faster scanners, more slices, and the

advent of dual source CT, the ability to resolve the coronary arteries via non-invasive imaging continues to progress [33]. Therefore, assessment and report of all incidental radiology findings has the potential to have a beneficial role in earlier diagnosis and clinical-decision making for ACS. This study examined patients with CTPE for suspicion of PTE, but CAC may also be relevant as a radiology finding in a variety of clinical scenarios and in different imaging examinations, which future studies could also assess.

Our study is unable to assess the impact of radiologic findings on ultimate management of the patients. A quality improvement study could be implemented to see if an intervention to increase incidental CAD reporting in the impression of radiologists' reports affects ACS diagnosis, clinical management, short term clinical outcomes, and long term clinical outcomes. Part of such a study could include surveying clinicians about the utility of radiologic impressions on management decisions in various clinical scenarios, particularly in regards to the diagnosis of ACS. We noticed that in some rare cases vague terminology is used to point out CAC. Some examples of this included "diffuse atherosclerotic changes" and "atherosclerotic change of the aorta great vessels." We think that avoiding a vague terminology might maximize clinical benefit. On the basis of our findings, we suggest follow up of patients with CAC to evaluate whether CAC corresponds to ACS or to chronic or undiagnosed CAD. In this study, we did not quantify the extent of CAC.

An interesting topic for future research is to evaluate the association of ACS with the extent and location of calcification in CAC positive patients. A recent study showed that in low-dose CT lung cancer screening, CAC scoring could be used as an independent predictor of cardiovascular events. Nevertheless, this can be limited by the presence of contrast agent in our study [34]. Our study demonstrated stronger associations of CAC with ACS in different patient populations. Potentially patterns of CAC location as well as extent of CAC and the CAC

score in various populations of patients could provide a more advanced predictive model of how likely the presence of CAC on imaging is associated with ACS in a given patient.

My Role

This study was completed through a coordinated effort of multiple individuals. My role included several components. I did a retrospective chart review of all 469 patients and generated a spreadsheet charting patient data and radiology reporting characteristics. I assisted with a portion of the data analysis, particularly looking at the reporting rates in the impression and Findings. Dr. Khalilzadeh was the primary statistician for the manuscript. I worked in conjunction with Dr. Choy and Dr. Khalilzadeh to draft the manuscript.

Conclusions

In conclusion, the results of this study showed that the presence of CAC is often not reported in the findings and especially the impression of pulmonary CT angiography studies of patients with suspected PTE. CAC is a significant predictor of ACS, particularly in younger patients (age < 70 years, especially men age ≤ 45 years old and women age ≤ 55 years old) and in patients without PTE, patients without a personal history of CAD, and those without cardiometabolic risk factors. Further prospective studies are needed to confirm these results and assess the impact of CAC on ACS diagnosis, short term clinical management, and long term clinical management. Our results apprise radiologists to assess and report CAC, particularly in the above subgroups of patients. We suggest that the presence or absence of CAC on CT pulmonary angiograms should be reported in the findings and impression of radiology reports.

A report of this work has been previously published (Johnson et. al 2014) [27].

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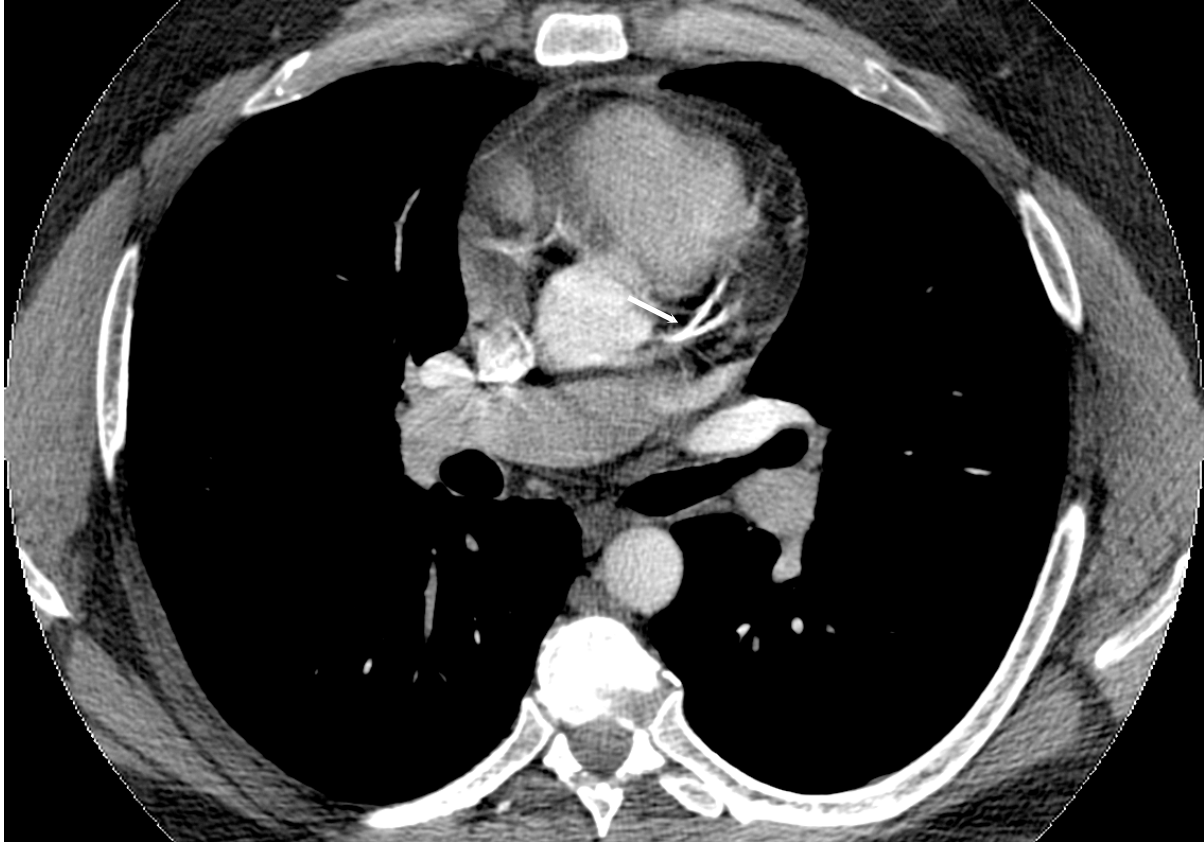


Figure 1

CT scan of a patient with suspected PTE and left coronary artery calcification (arrow). Calcification can be seen on left anterior descending and left circumflex arteries. This finding was not listed in the radiology report of the patient.

Table 1. Characteristics of the study participants

	Without coronary calcification (n=263)	With coronary calcification (n=206)	Total (n=469)	P
Age (years)	43.7±14.4	66.6±12.6	53.7±17.8	<0.001
Females	163 (63.0%)	96 (46.6%)	259 (55.2%)	0.001
PTE diagnosis	22 (8.4%)	30 (14.6%)	52 (11.1%)	0.034
ACS diagnosis	46 (17.5%)	59 (28.6%)	105 (22.4%)	<0.01
Past Medical History				
CAD	6 (2.3%)	48 (23.3%)	54 (11.5%)	<0.001
Myocardial Infarction	3 (1.1%)	27 (13.1%)	30 (6.4%)	<0.001
Stent placement	0 (0%)	6 (2.9%)	6 (1.3%)	0.007
Coronary artery bypass	0 (0%)	16 (7.8%)	16 (3.4%)	<0.001
Diabetes	19 (7.2%)	59 (28.8%)	78 (16.7%)	<0.001
Hyperlipidemia	34 (12.9%)	105 (51.0%)	139 (29.6%)	<0.001
Hypertension	56 (21.3%)	146 (70.9%)	202 (43.1%)	<0.001
Smoking	1 (0.4%)	10 (4.9%)	11 (2.3%)	0.002
Obesity	27 (10.3%)	28 (13.6%)	55 (10.7%)	0.267
Family History of CAD	10 (3.8%)	12 (5.8%)	22 (4.7%)	0.304
Coronary calcification in the radiology report	0 (0%)	114 (55.3%)	114 (24.3%)	-
Radiology findings	0 (0%)	114 (55.3%)	114 (24.3%)	-
Radiology impression	0 (0%)	9 (4.4%)	9 (1.9%)	-

Variables are presented as mean (SD) or number (percentage).

Table 2. Association of coronary artery calcification in CT pulmonary angiogram with ACS (n=469)

Positive CAC in different subgroups		Negative ACS	Positive ACS	OR (95% CI)	P
A)	Without past medical history of CAD (n=4)	114/327 (34.9%)	44/88 (50.0%)	1.9 (1.2-3.0)	0.009
	With past medical history of CAD (n=54)	33/37 (89.2%)	15/17 (88.2%)	0.9 (0.15-5.5)	0.917
B)	Without cardiac risk factors (n=200)	24/176 (13.6%)	9/24 (37.5%)	3.8 (1.5-9.6)	0.003
	With at least one cardiac risk factors ^a (n=269)	123/188 (65.4%)	50/81 (61.7%)	0.85 (0.5-1.5)	0.561
C)	Without PTE (n=417)	121/320 (37.8%)	55/97 (56.7%)	2.15 (1.4-3.4)	0.001
	With PTE (n=52)	26/44 (59.1%)	4/8 (50.0%)	0.7 (0.15-3.1)	0.632
D)	Age < 70 (n=377)	88/300 (29.3%)	38/77 (49.4%)	2.35 (1.4-3.9)	0.001
	Age ≥ 70 (n=92)	59/64 (92.2%)	21/28 (75.0%)	0.25 (0.1-0.9)	0.024
E)	Overall (n=469)	147/364 (40.4%)	59/105 (56.2%)	1.9 (1.2-2.9)	0.004

^a: Including diabetes, obesity, smoking, hypertension, and hyperlipidemia

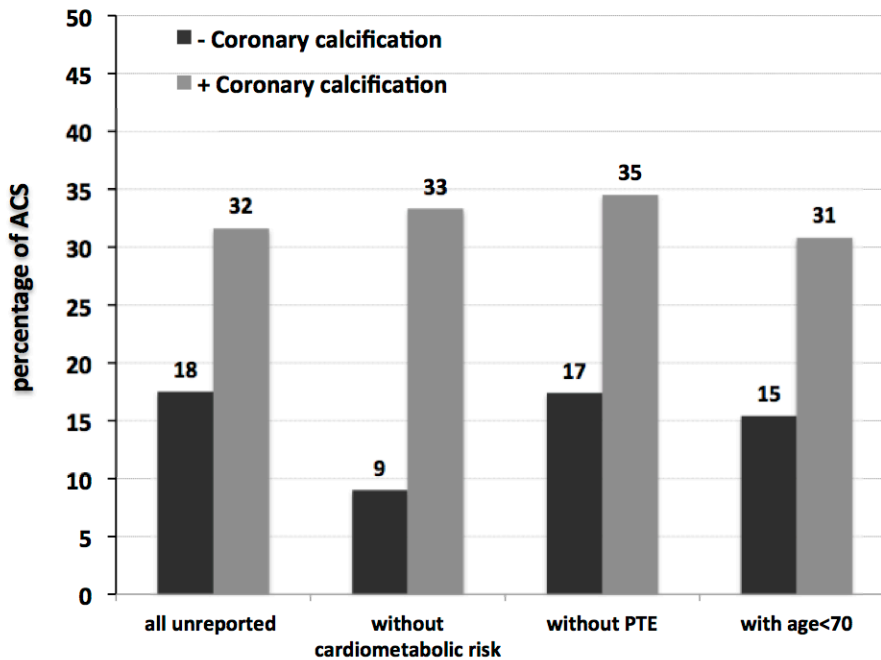


Figure 2

In patients with unreported CAC in the radiology assessment, there was a significant association between CAC in CT pulmonary angiogram and ACS (the first set on the left: OR=2.18, $p=0.004$). This association was more prominent in patients without cardiometabolic risk factors (OR=5.03, $p=0.002$); without PTE (OR=2.50, $p=0.001$); and with age <70 (OR=2.46; $p=0.004$).

Numbers above the columns are percentage.

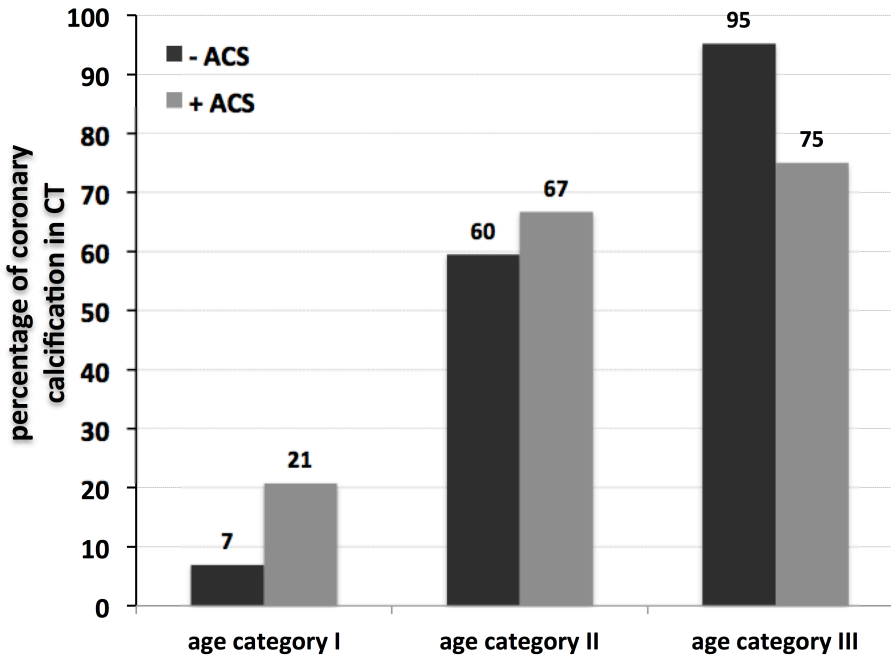


Figure 3

Association of coronary artery calcification in CT pulmonary angiogram and ACS in different age categories: I, age≤45 years in men and age≤55 years in women (n=203); II, 45 <age <70 years in men and 55< age<70 years in women (n=174); and III, age≥70 years in men and women (n=92).

There was a significant direct association in the youngest age category: OR=3.5, 95%CI=1.2-10.2, p=0.016). The association was significantly inversed in age category 3: OR=0.25, 95%CI=0.07-0.88; p=0.024. In age category 2 the association was positive but not significant: OR=1.4, 95%CI=0.7-2.7, p=0.38.

Numbers above the columns are percentage.

A report with these tables and figures has been published previously (Johnson et. al 2014) [27].